

NIH Global Health Interest Group, Seminar Series

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Seminar Title: International HIV Research: Past, Present and Future Global Health Research Opportunities

Presenter: Thomas C. Quinn MD, MSc, Associate Director for International Research, NIAID  
Summary and highlights by Travis Dittmer

Dr. Quinn presented his personal journey, beginning in the early 80's, during the time when the epidemiology of HIV transmission was starting to be dissected. He was puzzled by a spate of papers in MMWR (Morbidity and Mortality Weekly Report) reporting on cases of opportunistic infections, *Pneumocystis pneumonia* and Kaposi's Sarcoma in particular populations, including a group of Haitians living in the US. Dr. Quinn's start in HIV research began when he was in the right place at the right time. "I was fortunate to answer a request from Haiti to the Fogarty International Center, asking for a team to come down and see what was going on there", said Quinn. His team flew down to Haiti and after touring a hospital in Port-au-Prince was overwhelmed by the number of people suffering and dying from these mysterious and normally rare diseases (only a few cases had been seen in the US at that time). The team interviewed patients and a few things became immediately clear. It was a sexually transmitted disease since many spousal partners were affected. Also, the disease probably originated in Zaire (now the Democratic Republic of Congo) since many of the affected families had previously been there on visits. Peter Piot corroborated their theories by identifying a group of African patients in Belgium with similar symptoms that had also spent time in Zaire. Following these initial leads, Quinn and colleagues traveled to Kinshasa, Zaire (as part of Projet SIDA) and discovered a hospital filled with patients having basically the same disease as those in Port-au-Prince. "It was the first time in my career I was getting a dose of what international research was all about", said Quinn.

The team (now including Peter Piot) put together a report describing their discovery in Kinshasa and was dismayed when the NEJM rejected it without review because, as the editor put it, "this isn't relevant to Americans at this point." Fortunately the Lancet had a different view and published the first report out of Africa demonstrating a significant transmission of the then unknown disease in a large heterosexual population. They all realized they were uncovering something that hadn't been described before, but they still didn't know the cause.

To understand what the disease actually was, Dr. Quinn gathered together their collected blood samples and sent them to the Pasteur Institute in France where they eventually identified what is now known as HIV. This seminal work was published in Science and in 1986 he co-authored another article in that journal recommending that "prevention and control of HIV should be an immediate public health priority for all African countries, otherwise it will be a disaster." Fast-forward 30 years and there are now 65 million people infected, 34 million living with HIV and 31 million deaths caused by HIV. "This turned out to be one of the worst epidemics of our modern time", said Quinn, "and is especially sad since two-thirds of these cases are in Africa." He talked about how frustrating it was to publish these early papers and then see the disease being stigmatized and denied. With greater prevention efforts early on the epidemic might have been avoided.

Dr. Quinn emphasized the importance of cohorts in global health research because they move the science forward. He described the establishment in 1988 of a center in the rural Rakai district of Uganda to study HIV. Initially the center was set up as an epidemiological survey but then evolved into a long-standing cohort where ~15,000 people have been followed since 1988. Every year 12-15,000 household surveys are conducted and >60,000 blood samples have now been collected. The Rakai cohort was used for some of the earliest HIV clinical trials and in 2004 antiretroviral therapies became available to them through the help of PEPFAR. Dr. Quinn stressed that the Rakai cohort was essential for many of his key scientific discoveries and that it has been the backbone of countless research projects. With the Rakai cohort, “You could actually do global health in the field and continue to do basic science.... whatever you want to call it, it’s taking your developed lab skills and applying it to answer important scientific AND human disease issues.” The types of studies the Rakai cohort facilitates range from basic science, molecular epidemiology and clinical care to time trend analyses, observational research, randomized trials and operations research. Dr. Quinn recommended that for those pursuing research careers in global health to have a cohort.

Unsuccessful clinical trials can lead to new insights. By taking data from a “failed” STD clinical trial, Quinn and colleagues combined it with their extensive cohort database and made an important discovery about how HIV was transmitted. They already knew that 45% of HIV transmission occurred between married couples but could not account for the variability. By combining their HIV transmission data with data from their “failed” clinical trial on viral load (HIV RNA copies per ml) they discovered that the HIV viral load levels directly influence the transmission rate. If the viral load is low or even undetectable then the rate of transmission from that individual was essentially zero. Following on they also discovered that STD’s could enhance HIV transmission independently of HIV viral load. These studies helped give rise to the “treatment as prevention” theory and predicted that if new antiretroviral drugs could lower viral loads they in effect might lower transmission.

Circumcision lowers the HIV transmission rate. In a 2000 NEJM paper Quinn’s group showed that male partners of HIV-positive female partners could decrease their susceptibility of transmission through circumcision. Of the 137 uncircumcised men in their study, 40 became infected during a 2+ year period with an HIV-positive sex partner. In contrast, out of 50 circumcised men none became infected over the same time period. This pivotal study led to a series of related trials, which all confirmed that male circumcision is effective at reducing HIV infection and provided long-lasting protection against HIV infection. Related studies showed that the benefits of circumcision extend beyond that of reduce HIV infection.

Dr. Quinn discussed the significant clinical effects of antiretroviral therapies (ARTs) and concluded with the following points about them. The global progress on scaling-up the production of ARTs has been impressive such that reaching the WHO target of 15 million individuals on these therapies can be reached by 2015. Even so, disparities and inequities continue to exist in many countries and in key populations. In the past many countries simply had no choice so it is especially encouraging to see countries having to decide between strategies in dealing with the HIV epidemic, (e.g., early ART, “treatment as prevention”, pre-exposure prophylaxis). Antiretroviral therapies are powerful tools to combat the HIV epidemic but only if they’re accessible and people actually take them.

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For those interested in or thinking about a career in global health Dr. Quinn gave a quick run-through of organizations, collaborations and networks he thought one should be acquainted with.

- **NIAID Division of Intramural Research** – Many ongoing international projects (e.g. Peru, Brazil, Mali, Uganda, Tanzania, South Africa, China, India, Thailand, Cambodia, Korea) focusing on a range of research areas including HIV, tuberculosis, malaria, STDs and various neglected tropical diseases.
- **ICER (International Centers for Excellence in Research)** – Forms partnerships in developing countries to focus on critical global health problems such as HIV, tuberculosis, malaria and other vector-borne diseases. ICERs emphasize lab and field research in the development of new drugs, vaccines and other interventions as well as translational research to enable evaluation of new tools in collaboration with health officials in endemic areas. To complement these efforts the centers also focus on infrastructure development (including IT) and training.
- **International Collaborations for Global Research** – International Centers of Excellence in Research (ICER), International Centers for Infectious Diseases Research (ICIDR), Tropical Medicine Research Centers (TMRC), SEA Influenza Clinical Research Network, International Centers of Excellence in Malaria Research and Surveillance (ICEMRS), International Research in Infectious Diseases and AIDS (IRIDA), HVTN, HPTN, IMPACCT, ACTG, MTN, InSight, IeDEA, CFAR
- **Major NIAID-Funded HIV/AIDS Clinical Trials Networks** – AIDS Clinical Trials Group (ACTG), HIV Prevention Trials Network (HPTN), HIV Vaccine Trials Network (HVTN), International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT), International Network for Strategic Initiatives in Global HIV Trials (INSIGHT), Microbicide Trials Network (MTN)